REMARKS

I. Status of Claims

Claims 1-20 are pending.

II. Double Patenting

Claims 1-20 were subject to a provisional double patenting rejection under 35 U.S.C. §101 in view of the claims of U.S.S.N. 08/738,552. Applicants have permitted are U.S.S.N. 08/738,552 to become abandoned, obviating this rejection.

III. Rejections Under 35 U.S.C. §112, Second Paragraph

a) The Examiner has indicated that the term "surface" in claims 1, 2, 5 and 19 is confusing. Applicants have amended these claims, as well as claims 13 and 17, to replace the term "surface" with the phrase "solid support." Support for this amendment is found in the specification at, *e.g.*, page 5, lines 11-16. The adjective "solid" is included for clarity.

b) The Examiner indicates that it is not apparent what the purpose of treating the surface (now "solid support") with a DNA-inactivating agent. The rationale for using a DNA-inactivating agent is described in the specification at, *e.g.*, page 14, line 9 to page 15, line 9 . See also Example 6 (pages 25-26). Briefly, the DNA-inactivating destroys DNA in cells not protected by a solid plug. Applicants respectfully believe that the *claims* are clear and that, in view of this explanation, this rejection should be removed.

c) Claim has been amended to add the transitional phrase "comprising."

d) Claim 19 has been amended to add antecedent basis.

e) Claim 18 has been amended.

f) Claims 19 and 20 have been amended to correct typographical errors.

IV. Rejections Under 35 U.S.C. §103

a) Claims 1, 3, and 9 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Ornstein (U.S. Pat. No. 4,545,831) in view of Emmert-Buck *et al.*, 1996, *Science*, 274:998. Applicants respectfully traverse.

a

i) The Cited Art

Ornstein

Ornstein describes a method for processing of tape-mounted tissue sections, especially for transferring a thin tissue section from a flexible tape to a microscope slide. According to the method, a tissue section is adhered to a flexible tape (14). The tissue section is then contacted with a microscope slide (16) coated with an adhesive (18) that is photopolymerizable. Upon illumination of the entire slide, the entire section adheres to the polymerized adhesive and slide (18, 16). The flexible tape (14) is then removed.

Emmert-Buck et al.

Emmert-Buck *et al.* describes a method for isolating a small number of cells from a tissue section. According to the method described, a tissue section is adhered to a glass microscope slide. A thermoplastic film is placed over the tissue. Under microscopic inspection, the thermoplastic film is focally illuminated over an area of interest using an infrared laser. The infrared beam activates the thermoplastic film, which becomes focally adhesive. When the film is removed, selected cells remain adherent to the film surface (see, *e.g.*, Figure 1).

ii) The Traverse

The references cited do not support a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, the Examiner must indicate where the prior art provides reason or motivation for one of skill to make the claimed composition or carry out the claimed method. The Examiner must also demonstrate that one of ordinary skill would have had a reasonable expectation of success. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). References that serve merely as an invitation to experiment do not render an invention obvious. Moreover, in determining obviousness, prior art references must be read without benefit of the applicant's teachings. Applicants respectfully maintain that, in this case, the Examiner has failed to establish a *prima facie* case of obviousness.

The position advanced by the Examiner is that one of skill would have found motivation in the Emmert-Buck *et al.* reference to modify the method of Ornstein by "illuminating a covered cell population under microscopic vision and specifically focusing on the cell of interest." The Examiner concludes: "[t]herefore, a skilled artisan would have used a microscope to select a

cell in which a light source selectively focuses on a cell of interest covered with a photopolymerizable material under a microscope to form a solid cover attaching the cell." Applicants respectfully disagree.

The Examiner cites col. 5, lines 29-30 of Ornstein to support the *possibility* that the polymerized adhesive layer (18) used by Ornstein could be compatible with microscopic viewing prior to polymerization, although no such microscopic viewing is suggested by the reference. The section cited by the Examiner refers only use after polymerization and transfer of the entire tissue section. This is evident in the Ornstein patent both at col. 5, line 27 (same sentence as cited by the Examiner), which refers only to the *cured* layer (*i.e.*, for viewing *after* polymerization) and from the entire discussion by Ornstein. Although the Ornstein patent indicates that the *polymerized layer* should have a refractive index compatible with the slide and mounting medium (see, *e.g.*, col. 3, lines 17-20), there is no suggestion that the unpolymerized medium should have any particular refractive index. (In contrast, there is considerable teaching about the other properties, such as diffusion coefficients, of the unpolymerized material.)

Thus, nothing in Ornstein indicated that it would be possible or desirable to view cells through the unpolymerized layer. On the contrary, if, *arguendo*, a practitioner had attempted to microscopically visualize a particular cell using the Ornstein method, the attempt likely would have failed. The hypothetical practitioner would have been looking at a sandwich comprising a glass slide, an unpolymerized layer that could be opaque (*i.e.*, having unknown light transmission properties), the tissue section, and a pressure sensitive adhesive tape (which was likely opaque and, at best, would have had unknown light transmission qualities; see, *e.g.*, col. 1-2). Since Ornstein taught that the adhesive tape must be removed for viewing of the section, one of skill would have concluded that it was not possible to microscopically visualize individual cells through these materials. In short, nothing in Emmert-Buck et al. would have suggested that was possible or desirable to modify Ornstein's method to result in the presently claimed method. Clear, there could not have been any reasonable expectation of success that such visualization as is suggested by the Examiner could have been carried out.

Moreover, nothing in either of the references cited by the Examiner suggested that a photopolymerizable material could have been polymerized locally in a manner that would have allowed removal of a small diameter plug and a cell, or several cells, of interest. Emmert-Buck *et al.*, did not describe a photopolymerizable material. Instead, Emmert-Buck *et al.* described the use

of a infrared (*i.e.*, heat producing) laser and a thermoplastic material. Ornstein nowhere suggested that if was possible to photopolymerize a material over a small area of a few cells. Neither of the cited references suggested any mechanism by which such local polymerization could have been carried out. Again, nothing in the references suggested their combination, and if combined the combination would not have led to the presently claimed invention.

Thus, even if, *arguendo*, one of skill had been motivated to attempt to carry out the method of the present inventors, nothing in the cited references would have provided an expectation of success. Prior to the disclosure by the present inventors, it would not have been known whether it was even possible to locally polymerize a photopolymerizable material, remove unpolymerized material (not suggested by either of the cited references), and recover a single cell or small number of cells for further analysis.

The cited references provide no motivation to even try the method of the present invention. Even if, *arguendo*, one of skill had attempted to experiment, nothing in the references, individually or in combination, would have provided any expectation of success. Both motivation and the expectation of success can be found only in the present disclosure. Thus, Applicants respectfully request that this rejection be withdrawn.

b) Claims 2, 5-8, 10, and 13-18 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Ornstein (U.S. Pat. No. 4,545,831) in view of Emmert-Buck *et al.*, 1996, *Science*, 274:998, and Sekizawa *et al.*, 1996, *Neurology* 46:1350. Claims 4, and 11-12 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Ornstein (U.S. Pat. No. 4,545,831) in view of Emmert-Buck *et al.*, 1996, *Science*, 274:998, Sekizawa *et al.*, 1996, *Neurology* 46:1350, and Sandner *et al.* (U.S. Pat. No. 3,715,293). Applicants respectfully traverse.

Sekizawa *et al.* described PCR analysis using a single nucleated erythrocyte. Sandner *et al.* described that the photosensitizer 2,2-dimethoxy-2-phenyl acetone could be polymerized using non-ionizing radiation. Neither reference describes local polymerization of a photopolymerizable material, or use of such material in the isolation of a cell or group of cells.

Because Sekizawa *et al.* and Sandner *et al.* do not remedy the deficiencies of the underlying Ornstein and Emmert-Buck *et al.* references, as discussed *supra*, they fail to support a *prima facie* case of obviousness of claims 2, 4-8, and 10-14. Thus, Applicants respectfully request that these rejections be withdrawn.

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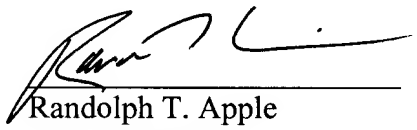
It is believed that the above amendments and remarks place the pending claims in condition of allowance. Issuance of a Notice of Allowance is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 326-2400, Ext. 5270.

Respectfully submitted,



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